```
=> d his nofile
```

```
(FILE 'HOME' ENTERED AT 10:48:36 ON 21 NOV 2006)
```

FILE 'HCAPLUS' ENTERED AT 10:48:46 ON 21 NOV 2006

E US2005-532690/APPS

L1 1 SEA ABB=ON PLU=ON US2005-532690/AP

E US2002-423253P/APPS

L2 1 SEA ABB=ON PLU=ON US2002-423253P/PRN

E WO2003-US34185/APPS

L*** DEL 0 S NL1-L3

L4 1 SEA ABB=ON PLU=ON (L1 OR L2 OR L3)

D SCAN

FILE 'REGISTRY' ENTERED AT 10:57:50 ON 21 NOV 2006

E 4-4-BENZYLOXY-3-CHLOROPHENYL-4-OXOBUTANOIC ACID

E 4-4-BENZYLOXY-3-CHLOROPHENYL-4-OXOBUTANOIC ACID/CN

E 4-BENZYLOXY-3-CHLOROPHENYL-4-OXOBUTANOIC ACID/CN

FILE 'HCAPLUS' ENTERED AT 10:59:07 ON 21 NOV 2006 SEL RN L4

FILE 'REGISTRY' ENTERED AT 10:59:17 ON 21 NOV 2006

L5 16 SEA ABB=ON PLU=ON (102513-61-1/BI OR 13335-57-4/BI OR

202577-82-0/BI OR 371251-24-0/BI OR 373596-81-7/BI OR 373596-82-8/BI OR 373596-84-0/BI OR 387844-34-0/BI OR 39208-08-7/BI OR 53090-45-2/BI OR 60525-32-8/BI OR 63539-02-6/BI OR 73083-19-9/B

I OR 74362-70-2/BI OR 74362-73-5/BI OR 77513-51-0/BI)

D SCAN

4 SEA ABB=ON PLU=ON L5 AND BUTANOIC

D SCAN

FILE 'REGISTRY' ENTERED AT 11:07:18 ON 21 NOV 2006

E BENZENEBUTANOIC ACID/CN

L7 1 SEA ABB=ON PLU=ON "BENZENEBUTANOIC ACID, ((3-CHLOROPHENYL)MET

HYLENE) HYDRAZIDE"/CN

D SCAN

E BENZENEBUTANOIC ACID/CN

L8 1 SEA ABB=ON PLU=ON "BENZENEBUTANOIC ACID"/CN

D SCAN

E BENZENEBUTANOIC ACID/CN

E BENZYLOXY/CN

L9 1 SEA ABB=ON PLU=ON BENZYLOXY/CN

D SCAN

FILE 'STNGUIDE' ENTERED AT 11:11:19 ON 21 NOV 2006

FILE 'REGISTRY' ENTERED AT 11:13:48 ON 21 NOV 2006

STRUCTURE UPLOADED

L11 1 SEA SSS SAM L10

FILE 'STNGUIDE' ENTERED AT 11:14:04 ON 21 NOV 2006

FILE 'REGISTRY' ENTERED AT 11:14:29 ON 21 NOV 2006

L12 STRUCTURE UPLOADED

L13 : 1 SEA SSS SAM L12

L14 8 SEA SSS FUL L12

D SCAN

L10

L6

```
1 SEA ABB=ON PLU=ON L5 AND L14
L15
               D SCAN
               SAVE L14 NANCY690/A TEMP
L16
             8 SEA ABB=ON PLU=ON (L14 OR L15)
     FILE 'HCAPLUS' ENTERED AT 11:16:08 ON 21 NOV 2006
L17
           4 SEA ABB=ON PLU=ON L16 (L) (THU OR PKT OR DMA OR PAC OR
               BAC)/RL
               D KWIC
               E DIABETES/CT
               E E3+ALL
               E E2+ALL
          2178 SEA ABB=ON PLU=ON "DIABETES INSIPIDUS"/CT
L18
L19
         12931 SEA ABB=ON PLU=ON "DIABETES INSIPIDUS"+OLD/CT
               E DIABETES/CT
               E E3+ALL
               E E3+ALL
L20
         75871 SEA ABB=ON PLU=ON "DIABETES MELLITUS"/CT
               E DIABETES/CT
               E E4+ALL
L21
         12931 SEA ABB=ON PLU=ON "DIABETES INSIPIDUS"+OLD/CT
               E DIABETES/CT
               E E7+ALL
L22
           297 SEA ABB=ON PLU=ON "DIABETES INSIPIDUS (L) NEPHROGENIC"/CT
        117864 SEA ABB=ON PLU=ON ?DIABETES?
L23
               E ATHEROSCLEROSIS/CT
               E E3+ALL
L24
         37882 SEA ABB=ON PLU=ON ATHEROSCLEROSIS+OLD/CT
               E ATHEROSCLEROSIS/CT
               E ARTERIOSCLEROSIS/CT
               E E3+ALL
L25
         41547 SEA ABB=ON PLU=ON ARTERIOSCLEROSIS+NT/CT
               E ARTERIOSCLEROSIS/CT
               E E4+ALL
               E OBESITY/CT
               E E3+ALL
L26
         28762 SEA ABB=ON PLU=ON OBESITY+NT/CT
               E HYPERTENSION/CT
               E E3+ALL
         51377 SEA ABB=ON PLU=ON HYPERTENSION/CT
L27
               E FATTY LIVER DISEASE/CT
               E E3+ALL
               E E2+ALL
         11032 SEA ABB=ON PLU=ON "LIVER, DISEASE (L) FATTY"+OLD/CT
L28
               E NEPHROPATHY/CT
               E E3+ALL
               E E2+ALL
L29
         40906 SEA ABB=ON PLU=ON "KIDNEY, DISEASE"+OLD+NT/CT
L30
         68189 SEA ABB=ON PLU=ON "KIDNEY, DISEASE"+OLD, NT/CT
               E RETINOPATHY/CT
               E E3+ALL
               E E2+ALL
          7915 SEA ABB=ON PLU=ON "EYE, DISEASE (L) RETINOPATHY"+OLD/CT
L31
               E FOOT ULCERATION/CT
               E FOOT /CT
               E E+ALL
               E E3+ALL
               E FOOT/CT
               E E3+ALL
```

```
E ULCERATION/CT
                E CATARACT/CT
                E E3+ALL
L32
           5862 SEA ABB=ON PLU=ON CATARACT+OLD/CT
                E CATARACT/CT
                E E4+ALL
                E HYPERLIPIDEMIA/CT
                E E3+ALL
L33
          11861 SEA ABB=ON PLU=ON HYPERLIPIDEMIA+OLD, NT/CT
                E CACHEXIA/CT
                E E3+ALL
L34
           2566 SEA ABB=ON PLU=ON CACHEXIA/CT
L35
         234979 SEA ABB=ON PLU=ON FATTY LIVER DISEASE? OR FOOT ULCER? OR
                FEET ULCER? OR INSULIN RESISTANCE? OR OBESITY? OR HYPERLIPIDEMI
                ? OR ATHEROSCLERO? OR ARTERIOSCLER? OR HYPERTENS? OR NEPHROPATH
                ? OR NEUROPATH? OR RETINOPATH? OR CACHEXÍA
L36
         381179 SEA ABB=ON PLU=ON (L18 OR L19:OR L20 OR L21 OR L22 OR L23 OR
                L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR
                L33 OR L34 OR L35)
L37
              3 SEA ABB=ON PLU=ON L36 AND L17
L38
              5 SEA ABB=ON PLU=ON L16 AND L36
L39
              5 SEA ABB=ON PLU=ON
                                   (L37 OR L38)
                D KWIC
L40
              4 SEA ABB=ON PLU=ON L39 NOT L4
                E HODGE K/AU
L41
            12 SEA ABB=ON PLU=ON ("HODGE K"/AU OR "HODGE KIRVIN L"/AU)
                E SHARMA S/AU
L42
          3442 SEA ABB=ON PLU=ON ("SHARMA S"/AU OR "SHARMA S A"/AU OR
                "SHARMA S A N"/AU OR "SHARMA S AMITA"/AU OR "SHARMA S B"/AU OR
                "SHARMA S C"/AU OR "SHARMA S C L"/AU OR "SHARMA S CHIDANANDA"/A
                U OR "SHARMA S D"/AU OR "SHARMA S D GURUMAYUM"/AU OR "SHARMA S
                DAS"/AU OR "SHARMA S G"/AU OR "SHARMA S H K"/AU OR "SHARMA S
                J"/AU OR "SHARMA S K"/AU OR "SHARMA S KUMAR"/AU OR "SHARMA S
                L"/AU OR "SHARMA S M"/AU OR "SHARMA S N"/AU OR "SHARMA S P"/AU
                OR "SHARMA S R"/AU OR "SHARMA S RAMA GOPAL"/AU OR "SHARMA S
                S"/AU OR "SHARMA S SEN"/AU OR "SHARMA S SHELLEY"/AU OR "SHARMA
                S SHELLY"/AU OR "SHARMA S V"/AU OR "SHARMA SHALINI"/AU)
                E VON BORSTEL R/AU
            114 SEA ABB=ON PLU=ON ("VON BORSTEL R"/AU OR "VON BORSTEL R
L43
                C"/AU OR "VON BORSTEL REID"/AU OR "VON BORSTEL REID W"/AU OR
                "VON BORSTEL REID WARREN"/AU)
                E VONBORSTEL R/AU
L44
              2 SEA ABB=ON PLU=ON "VONBORSTEL REID W"/AU
            116 SEA ABB=ON PLU=ON (L43 OR L44)
L45
                E WOLPE S/AU
             33 SEA ABB=ON PLU=ON ("WOLPE S"/AU OR "WOLPE S D"/AU OR "WOLPE
L46
                STEPHEN"/AU OR "WOLPE STEPHEN D"/AU OR "WOLPE STEVE D"/AU OR
                "WOLPE STEVEN"/AU)
L47
              7 SEA ABB=ON PLU=ON (L41 AND (L42 OR L45 OR L46)) OR (L42 AND
                (L45 OR L46)) OR (L45 AND L46)
L48
              4 SEA ABB=ON PLU=ON L40 NOT L47
     FILE 'MEDLINE' ENTERED AT 11:28:39 ON 21 NOV 2006
     FILE 'HCAPLUS' ENTERED AT 11:29:02 ON 21 NOV 2006
L49
             6 SEA ABB=ON PLU=ON (L17 OR L48)
L50
              5 SEA ABB=ON
                          PLU=ON L49 NOT (L47 OR L4)
     FILE 'MEDLINE' ENTERED AT 11:29:39 ON 21 NOV 2006
```

```
L51
            O SEA ABB=ON PLU=ON L16
     FILE 'EMBASE, BIOSIS, CAOLD' ENTERED AT 11:29:56 ON:21 NOV 2006
L52
           0 SEA ABB=ON PLU=ON L16
     FILE 'WPIX' ENTERED AT 11:30:02 ON 21 NOV 2006
L53
           1 SEA SSS FUL L12
     FILE 'REGISTRY' ENTERED AT 11:30:42 ON 21 NOV 2006
              D BROWSE L15
             0 SEA ABB=ON PLU=ON 74362-73-5/CRN
L54
     FILE 'HCAPLUS' ENTERED AT 11:31:18 ON 21 NOV 2006
           2 SEA ABB=ON PLU=ON L15
L55
             7 SEA ABB=ON PLU=ON (L55 OR L50)
L56
             6 SEA ABB=ON PLU=ON L56 NOT (L47 OR L4)
L57
     FILE 'MEDLINE, EMBASE, BIOSIS, CAOLD' ENTERED AT 11:31:55 ON 21 NOV 2006
        O SEA ABB=ON PLU=ON L15
L58
     FILE 'WPIX' ENTERED AT 11:32:13 ON 21 NOV 2006
     FILE 'REGISTRY' ENTERED AT 11:32:24 ON 21 NOV 2006
               D BROWSE L15
     FILE 'WPIX' ENTERED AT 11:32:39 ON 21 NOV 2006
L59
             O SEA ABB=ON PLU=ON BENZENEBUTANOIC ACID/CN
               E BENZENEBUTANOIC ACID, 3-CHLORO-Γ-ΟΧΟ-4-(PHENYLMETHOXY)-
    FILE 'HCAPLUS' ENTERED AT 11:33:15 ON 21 NOV 2006
           1 S L1
L60
             8 SEA ABB=ON PLU=ON L16
             1 SEA ABB=ON PLU=ON L60 NOT (L57 OR L47 OR L1)
L61
            1 SEA ABB=ON PLU=ON L60 NOT (L57 OR L47 OR L4)
L62
               D KWIC
            7 SEA ABB=ON PLU=ON (L61 OR L62 OR L57)
            O SEA ABB=ON PLU=ON L60 NOT (L63 OR L47 OR L4)
L64
    FILE 'HCAPLUS' ENTERED AT 11:34:17 ON 21 NOV 2006
     FILE 'WPIX' ENTERED AT 11:34:23 ON 21 NOV 2006
               D OUE L47
               D OUE L63
               D OUE L53
    FILE 'STNGUIDE' ENTERED AT 11:34:37 ON 21 NOV 2006
     FILE 'HCAPLUS, WPIX' ENTERED AT 11:34:47 ON 21 NOV 2006
L65
            15 DUP REM L47 L63 L53 (0 DUPLICATES REMOVED)
                    ANSWERS '1-14' FROM FILE HCAPLUS
                    ANSWER '15' FROM FILE WPIX
     FILE 'WPIX' ENTERED AT 11:35:04 ON 21 NOV 2006
L66
             1 SEA ABB=ON PLU=ON L53/DCR
               SEL SDCN L53
               EDIT E1 SDCN DCN
L67
             1 SEA ABB=ON PLU=ON RAECKI/DCN
               SEL DCSE L53
               EDIT E2 DCSE DCRE
```

FILE 'HCAPLUS' ENTERED AT 11:36:48 ON 21 NOV 2006

FILE 'WPIX' ENTERED AT 11:36:53 ON 21 NOV 2006

D QUE L47

D OUE L63

D QUE L53

D QUE L69

FILE 'STNGUIDE' ENTERED AT 11:37:03 ON 21 NOV 2006

FILE 'HCAPLUS, WPIX' ENTERED AT 11:37:12 ON 21 NOV 2006
L70

15 DUP REM L47 L63 L53 L69 (1 DUPLICATE REMOVED)
ANSWERS '1-14' FROM FILE HCAPLUS
ANSWER '15' FROM FILE WPIX

D IBIB ABS HITIND HITSTR RETABLE L70 1-14

D IDE L53 TOT

D ALL ABEQ TECH L70 TOT

FILE 'WPIX' ENTERED AT 11:38:52 ON 21 NOV 2006
D ALL ABEQ TECH L69 TOT

FILE 'REGISTRY' ENTERED AT 12:02:33 ON 21 NOV 2006 D BROWSE L15

FILE 'REGISTRY' ENTERED AT 12:02:51 ON 21 NOV 2006

L71 STR 74362-73-5

L72 1 SEA FAM FUL L71

D SCAN

L73 STRUCTURE UPLOADED

L74 1 SEA SSS SAM L73

L75 8 SEA SSS FUL L73

L76 8 SEA ABB=ON PLU=ON (L75 OR L14)

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 11:36:48 ON 21 NOV 2006
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=> file wpix:

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DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

20 NOV 2006 <20061120/UP>

200674 <200674/DW>

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=> d que 147

L41 12 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HODGE K"/AU OR "HODGE KIRVIN L"/AU)

L42

3442 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SHARMA S"/AU OR "SHARMA S A"/AU OR "SHARMA S A N"/AU OR "SHARMA S AMITA"/AU OR "SHARMA S B"/AU OR "SHARMA S C"/AU OR "SHARMA S C L"/AU OR "SHARMA S CHIDANANDA"/AU OR "SHARMA S D"/AU OR "SHARMA S D GURUMAYUM"/AU OR "SHARMA S DAS"/AU OR "SHARMA S G"/AU OR "SHARMA S H K"/AU OR "SHARMA S J"/AU OR "SHARMA S K"/AU OR "SHARMA S KUMAR"/AU OR "SHARMA S L"/AU OR "SHARMA S M"/AU OR "SHARMA S N"/AU OR "SHARMA S P"/AU OR "SHARMA S RAMA GOPAL"/AU OR "SHARMA S S"/AU OR "SHARMA S SHELLEY"/AU OR "SHARMA S SHALLINI"/AU)

L43

114 SEA FILE=HCAPLUS ABB=ON PLU=ON: ("VON BORSTEL R"/AU OR "VON BORSTEL R C"/AU OR "VON BORSTEL REID"/AU OR "VON BORSTEL REID W"/AU OR "VON BORSTEL REID WARREN"/AU)

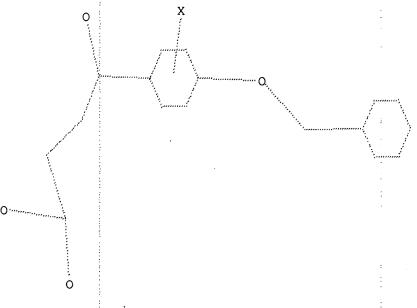
2 SEA FILE=HCAPLUS ABB=ON PLU=ON "VONBOR\$TEL REID W"/AU

L45 116 SEA FILE=HCAPLUS ABB=ON PLU=ON (L43 OR L44)

L46 33 SEA FILE=HCAPLUS ABB=ON PLU=ON ("WOLPE S"/AU OR "WOLPE S D"/AU OR "WOLPE STEPHEN"/AU OR "WOLPE STEPHEN D"/AU OR "WOLPE

L44

```
STEVE D"/AU OR "WOLPE STEVEN"/AU)
L47
              7 SEA FILE=HCAPLUS ABB=ON PLU=ON (L41 AND (L42 OR L45 OR L46))
               OR (L42 AND (L45 OR L46)) OR (L45 AND L46)
=> d que 163
             1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2005-532690/AP
L2
             1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2002-423253P/PRN
L3
             1 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                (WO2003-US34185/AP OR
               WO2003-US34185/PRN)
L4
             1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3)
L5
            16 SEA FILE=REGISTRY ABB=ON PLU=ON (102513-61-1/BI OR 13335-57-4
                /BI OR 202577-82-0/BI OR 371251-24-0/BI OR 373596-81-7/BI OR
               373596-82-8/BI OR 373596-84-0/BI OR 387844-34-0/BI OR 39208-08-
               7/BI OR 53090-45-2/BI OR 60525-32-8/BI OR 63539-02-6/BI OR
               73083-19-9/BI OR 74362-70-2/BI OR 74362-73-5/BI OR 77513-51-0/B
               I)
L12
               STR
```

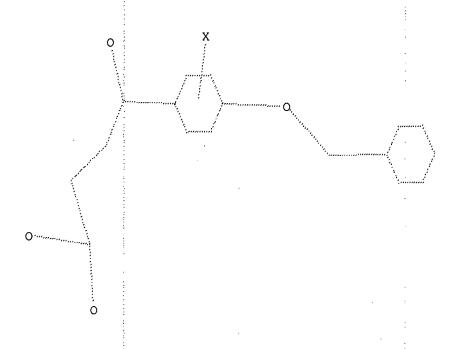


| Structure | attril | outes | s must be viewed usin | g STN Ex | press query preparation. |
|-----------|--------|-------|-----------------------|----------|-------------------------------|
| L14 | | | FILE=REGISTRY SSS FU | _ | |
| L15 | 1 | SEA | FILE=REGISTRY ABB=ON | PLU=ON | L5 AND L14 |
| L16 | : 8 | SEA | FILE=REGISTRY ABB=ON | PLU=ON | (L14 OR L15) |
| L17 | 4 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON . | L16 (L) (THU OR PKT OR DMA OR |
| | : | PAC | OR BAC)/RL | : | |
| L18 | 2178 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON | "DIABETES INSIPIDUS"/CT |
| L19 | 12931 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON : | "DIABETES INSIPIDUS"+OLD/CT |
| L20 | 75871 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON . | "DIABETES MELLITUS"/CT |
| L21 | 12931 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON : | "DIABETES INSIPIDUS"+OLD/CT |
| L22 | 297 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON | "DIABETES INSIPIDUS (L) |
| | | NEP | HROGENIC"/CT | | |
| L23 | 117864 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON | ?DIÁBETES? |
| L24 | 37882 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON | ATHEROSCLEROSIS+OLD/CT |
| L25 | 41547 | SEA | FILE=HCAPLUS ABB=ON | PLU=ON | ARTERIOSCLEROSIS+NT/CT |

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L26
          28762 SEA FILE=HCAPLUS ABB=ON PLU=ON OBESITY+NT/CT
L27
          51377 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 HYPERTENSION/CT
L28
          11032 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                  "LIVER, DISEASE (L) FATTY"+OLD
                /CT
L29
          40906 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                  "KIDNEY, DISEASE"+OLD+NT/CT
L30
                                                  "KIDNEY, DISEASE"+OLD, NT/CT
          68189 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
L31
           7915 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                  "EYE, DISEASE (L) RETINOPATHY"
                +OLD/CT
L32
           5862 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON: CATARACT+OLD/CT
L33
          11861 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON: HYPERLIPIDEMIA+OLD, NT/CT
L34
           2566 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                 CACHEXIA/CT
L35
         234979 SEA FILE=HCAPLUS ABB=ON PLU=ON FATTY LIVER DISEASE? OR FOOT
                ULCER? OR FEET ULCER? OR INSULIN RESISTANCE? OR OBESITY? OR
                HYPERLIPIDEMI? OR ATHEROSCLERO? OR ARTERIOSCLER? OR HYPERTENS?
                OR NEPHROPATH? OR NEUROPATH? OR RETINOPATH? OR CACHEXIA
L36
         381179 SEA FILE=HCAPLUS ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21 OR
                L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR
                L31 OR L32 OR L33 OR L34 OR L35)
              3 SEA FILE=HCAPLUS ABB=ON PLU=ON
L37
                                                 L36 AND L17
L38
              5 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 L16 AND L36
L39
             5 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 (L37 OR L38)
                                         PLU=ON L39 NOT L4
L40
             4 SEA FILE=HCAPLUS ABB=ON
L41
            12 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON ("HODGE K"/AU OR "HODGE
                KIRVIN L"/AU)
           3442 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SHARMA S"/AU OR "SHARMA S
L42
                A"/AU OR "SHARMA S A N"/AU OR "SHARMA S AMITA"/AU OR "SHARMA S
                B"/AU OR "SHARMA S C"/AU OR "SHARMA S C L"/AU OR "SHARMA S
                CHIDANANDA"/AU OR "SHARMA S D"/AU OR "SHARMA S D GURUMAYUM"/AU
                OR "SHARMA S DAS"/AU OR "SHARMA S G"/AU OR "SHARMA S H K"/AU
                OR "SHARMA S J"/AU OR "SHARMA S K"/AU OR "SHARMA S KUMAR"/AU
                OR "SHARMA S L"/AU OR "SHARMA S M"/AU OR "SHARMA S N"/AU OR
                "SHARMA S P"/AU OR "SHARMA S R"/AU OR "SHARMA S RAMA GOPAL"/AU
                OR "SHARMA S S"/AU OR "SHARMA S SEN"/AU OR "SHARMA S SHELLEY"/A
                U OR "SHARMA S SHELLY"/AU OR "SHARMA S V"/AU OR "SHARMA
                SHALINI"/AU)
L43
            114 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                 ("VON BORSTEL R"/AU OR "VON
                BORSTEL R C"/AU OR "VON BORSTEL REID"/AU OR "VON BORSTEL REID
                W"/AU OR "VON BORSTEL REID WARREN"/AU)
L44
              2 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                 "VONBORSTEL REID W"/AU
            116 SEA FILE=HCAPLUS ABB=ON PLU=ON (L43 OR L44)
L45
L46
             33 SEA FILE=HCAPLUS ABB=ON PLU=ON: ("WOLPE'S"/AU OR "WOLPE S
                D"/AU OR "WOLPE STEPHEN"/AU OR "WOLPE STEPHEN D"/AU OR "WOLPE
                STEVE D"/AU OR "WOLPE STEVEN"/AU)
L47
              7 SEA FILE=HCAPLUS ABB=ON PLU=ON (L41 AND (L42 OR L45 OR L46))
                OR (L42 AND (L45 OR L46)) OR (L45 AND L46)
L48
              4 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 NOT L47
L49
              6 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                 (L17 OR:L48)
L50
              5 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 NOT (L47 OR L4)
            2 SEA FILE=HCAPLUS ABB=ON
7 SEA FILE=HCAPLUS ABB=ON
L55
                                         PLU=ON L15
L56
                                         PLU=ON (L55 OR L50)
L57
             6 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON L56 NOT (L47 OR L4)
L60
             8 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON L16
                                         PLU=ON: L60 NOT (L57 OR L47 OR L1)
L61
            1 SEA FILE=HCAPLUS ABB=ON
L62
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                                         PLU=ON L60 NOT (L57 OR L47 OR L4)
L63
              7 SEA FILE=HCAPLUS ABB=ON PLU=ON: (L61 OR:L62 OR L57)
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=> d que 153 L12

STR



Structure attributes must be viewed using STN Express query preparation. L53 1 SEA FILE=WPIX SSS FUL L12

=> d que 169

L67 1 SEA FILE=WPIX ABB=ON PLU=ON RAECKI/DCN
L68 0 SEA FILE=WPIX ABB=ON PLU=ON 905973-0-0-0/DCRE

L69 1 SEA FILE=WPIX ABB=ON PLU=ON (L67 OR L68)

=> file stnguide

FILE 'STNGUIDE' ENTERED AT 11:37:03 ON 21 NOV 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov 17, 2006 (20061117/UP).

=> dup rem 147,163,153,169

FILE 'HCAPLUS' ENTERED AT 11:37:12 ON 21 NOV 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIX' ENTERED AT 11:37:12 ON 21 NOV 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L69
L70

15 DUP REM L47 L63 L53 L69 (1 DUPLICA)

15 DUP REM L47 L63 L53 L69 (1 DUPLICATE REMOVED)
ANSWERS '1-14' FROM FILE HCAPLUS

ANSWER '15' FROM FILE WPIX

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=> d ibib abs hitind hitstr retable 170 1-14;d ide 153 tot ;d all abeq tech 170 tot
L70 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:
                         2004:412751 HCAPLUS <<LOGINID::20061121>>
DOCUMENT NUMBER:
                         140:400084
TITLE:
                         Oxocarboxylic acids and esters thereof for the
                         treatment of metabolic disorders
INVENTOR(S):
                         Hodge, Kirvin L.; Sharma, Shalini;
                         Von Borstel, Reid W.; Wolpe, Stephen
                         Wellstat Therapeutics Corporation, USA; Von Borstel,
PATENT ASSIGNEE(S):
                         Reid W.
SOURCE:
                         PCT Int. Appl., 22 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
                                            _____
     WO 2004041165
                                            WO 2003-US34185
                          A2
                                20040521
                                                                   20031028
     WO 2004041165
                         АЗ
                                20050203
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20040521
     CA 2502297
                                            CA 2003-2502297
                          AA
                                                                   20031028
     AU 2003286728
                                20040607
                          A1
                                            AU 2003-286728
                                                                   20031028
     EP 1556085
                                20050727
                                            EP 2003-777939
                          A2
                                                                   20031028
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006507303
                          Т2
                                20060302
                                            JP 2004-550151
                                                                   20031028
     US 2006035970
                          Α1
                                20060216
                                            US 2005-532690
                                                                   20050426
PRIORITY APPLN. INFO.:
                                            US 2002-423253P
                                                                P. 20021101
                                                                W 20031028
                                            WO 2003-US34185
     Oxocarboxylic acids and esters thereof are disclosed which are useful for
AB
     the treatment of various metabolic disorders, e.g. insulin resistance
     syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia,
     obesity, atherosclerosis and arteriosclerosis.
IC
     ICM A61K
CC
     1-10 (Pharmacology)
L70 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
                         2005:177884 HCAPLUS <<LOGINID::20061121>>
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         142:279944
TITLE:
                         Preparation of phenyl thioethers for the treatment of
                         metabolic disorders
INVENTOR(S):
                         Sharma, Shalini; Von Borstel, Reid
                         W.; Hodge, Kirvin L.
```

Wellstat Therapeutics Corporation, USA

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

1 .

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND DATE | APPLICATION NO. | DATE |
|------------------------|-----------------|---------------------------------|-----------------|
| WO 2005018628 | A1 20050303 | WO 2004-US26561 | 20040816 |
| W: AE, AG, AL, | AM, AT, AU, AZ, | BA, BB, BG, BR, BW, | BY, BZ, CA, CH, |
| CN, CO, CR, | CU, CZ, DE, DK, | DM, DZ, EC, EE, EG, | ES, FI, GB, GD, |
| GE, GH, GM, | HR, HU, ID, IL, | IN, IS, JP, KE, KG, | KP, KR, KZ, LC, |
| LK, LR, LS, | LT, LU, LV, MA, | MD, MG, MK, MN, MW, | MX, MZ, NA, NI, |
| NO, NZ, OM, | PG, PH, PL, PT, | RO, RU, SC, SD, SE, | SG, SK, SL, SY, |
| TJ, TM, TN, | TR, TT, TZ, UA, | UG, US, UZ, VC, VN, | YU, ZA, ZM, ZW |
| RW: BW, GH, GM, | KE, LS, MW, MZ, | NA, SD, SL, SZ, TZ, | UG, ZM, ZW, AM, |
| AZ, BY, KG, | KZ, MD, RU, TJ, | TM, AT, BE, BG, CH, | CY, CZ, DE, DK, |
| EE, ES, FI, | FR, GB, GR, HU, | IE, IT, LU, MC, NL, | PL, PT, RO, SE, |
| SI, SK, TR, | BF, BJ, CF, CG, | CI, CM, GA, GN, GQ, | GW, ML, MR, NE, |
| SN, TD, TG | | | |
| AU 2004266673 | A1 20050303 | AU 2004-266673 | 20040816 |
| CA 2533890 | AA 20050303 | CA 2004-2533890 | 20040816 |
| EP 1656127 | A1 20060517 | EP 2004-781277 | 20040816 |
| R: AT, BE, CH, | DE, DK, ES, FR, | GB, GR, IT, LI, LU, | NL, SE, MC, PT, |
| IE, SI, FI, | RO, CY, TR, BG, | CZ, EE, HU, PL, SK | |
| CN 1835743 | A 20060920 | CN 2004-80023552 | 20040816 |
| NO 2006000502 | A 20060503 | CN 2004-80023552 NO 2006-502 | 20060131 |
| PRIORITY APPLN. INFO.: | | US 2003-496533P | P 20030820 |
| | | WO 2004-US26561 | W 20040816 |
| OTHER SOURCE(S): | CASREACT 142:27 | 9944; MARPAT 142:2799 | 344 |
| GI | | | |

AΒ The title compds. I [n = 1-2; m, q, t = 0-1; R5 = alkyl; R9 = H, halo,

alkyl, alkoxy; A = (un)substituted Ph, cycloalkyl, 5-6 membered heteroarom. ring having 1 or 2 ring heteroatoms selected from N, S and O and the heteroarom. ring is covalently bound to the remainder of the compound I by a ring carbon; X = CH2; Q = OR1 and R1 = Me, Et; or X = CH2CR12R13 or CH2CH(NHAc) (wherein R12, R13 = H, Me), Q = OR1 and R1 = H, alkyl; or X = CH2CH2 and Q = NR10R11 (wherein one of R10 and R11 = H, alkyl or OH, and the other = H); alternatively, when R1 = H, the biol. active agent can be a pharmaceutically acceptable salt of the compound I], useful for the treatment of various metabolic disorders, such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis are disclosed. E.g., a multi-step synthesis of II, starting from 2,6-dimethylbenzyl alc., was given. The pharmaceutical composition comprising the compound I is also disclosed.

IC ICM A61K031-19

ICS A61K031-235; C07C323-00

CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds) Section cross-reference(s): 1, 63

RETABLE

L70 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:962218 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER:

143:266913

TITLE:

Preparation of 3-pyrazolecarboxamide derivatives as

CB1 receptor modulators for the treatment of

obesity and other diseases

INVENTOR(S):

Cheng, Leifeng; Lindstedt-Alstermark, Eva-Lotte;

Boije, Anna Maria Persdotter

PATENT ASSIGNEE(S):

SOURCE:

Astrazeneca AB, Swed.; Astrazeneca UK Limited

PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | TENT | NO. | | | KIN | D | DATE | | | APPL | ICAT: | ION N | 0. | | D | ATE | | |
|----|------|-------|-----|-----|-----|-----|------|------|-----|------|-------|-------|-----|-----|-----|------|-----|----|
| | 2005 | | | | | | 2005 | 0901 | | WO 2 | 005- | GB534 | | | 2 | 0050 | 216 | |
| WO | 2005 | 60803 | 43 | | A3 | | 2006 | 0112 | | • | | | | | | | | |
| | W: | AE, | AG, | AL, | AM, | AT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, | |
| | | | | | | | | | | | | EE, | | | | | | |
| | | | | | | | | | | | | KE, | | | | | | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, | |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | |
| | | | | | | | | | | | | VC, | | | | | | sm |
| | RW: | • | | | | | | | | | | SZ, | | | | | - | |
| | | AZ, | BY, | KG, | KZ, | MD, | RU, | TJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | |
| | | EE, | ES, | FI, | FR, | GB, | GR, | HU, | IE, | IS, | IT, | LT, | LU, | MC, | NL, | PL, | PT, | |
| | | RO, | SE, | SI, | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | |
| | | MR, | NE, | SN, | TD, | TG | | | | : | | | | • | | | • | |
| ΑU | 2005 | 2141 | 30 | | A1 | | 2005 | 0901 | | AU 2 | 005- | 21413 | 0 | | 2 | 0050 | 216 | |
| CA | 2555 | 331 | | | AA | | 2005 | 0901 | | CA 2 | 005- | 25553 | 31 | • | 2 | 0050 | 216 | |
| ΕP | 1718 | 617 | | | A2 | | 2006 | 1108 | | EP 2 | 005~ | 71773 | 0 | | 2 | 0050 | 216 | |
| | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR. | IT. | LI, | LU, | NL, | SE, | MC, | PT, | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

NO 2006003787 A 20060919 NO 2006-3787 20060824
PRIORITY APPLN. INFO.: GB 2004-3779 A 20040220

GB 2004-20780 A 20040918 WO 2005-GB534 W 20050216

OTHER SOURCE(S): MARPAT 143:266913

GI

AB The title compds. I [R1 = substituted alkoxy, sulfonyl, sulfonamide or silanyl; Ra = halo, alkyl or alkoxy; m, n = 0-3; R2 = alkyl, alkoxy, etc.; R3 = substituted aminocarbonyl, etc.; R4 = H, alkyl, etc., with two exclusions, and pharmaceutically acceptable salts thereof] were prepared as CB1 receptor modulators. As an example, II was synthesized via sulfonylation of the corresponding phenol (preparation given) with n-PrSO2Cl in 49% yield. I are active in the CB1 receptor with IC50 values of < 1 μM (IC50 = 6 nM for II) and believed to be selective CB1 antagonists or inverse agonists. Therefore, I and their pharmaceutical compns. may be used in the treatment of *obesity*, psychiatric disorders, neurol. disorders and so on.

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

ST pyrazolecarboxamide prepn *obesity* psychiatric neurol disorder treatment; CB1 receptor modulator pyrazole carboxamide prepn

IT Nervous system, disease

ICM C07D231-00

(Huntington's chorea, treatment of; preparation of pyrazolecarboxamides CB1 receptor modulators for treatment of *obesity* and other diseases)

IT Mental and behavioral disorders

(attention deficit disorder, treatment of; preparation of pyrazolecarboxamides CB1 receptor modulators for treatment of **obesity** and other diseases)

IT Mental and behavioral disorders

(bipolar disorder, treatment of; preparation of pyrazolecarboxamides CB1 receptor modulators for treatment of *obesity* and other

IC

```
diseases)
IT
     Mental and behavioral disorders
        (dementia, treatment of; preparation of pyrazolecarboxamides CB1 receptor
        modulators for treatment of obesity and other diseases)
ΙT
     Mental and behavioral disorders
        (depression, treatment of; preparation of pyrazolecarboxamides CB1 receptor
        modulators for treatment of obesity and other diseases)
ΙT
     Mental and behavioral disorders
        (obsession-compulsion, treatment of; preparation of pyrazolecarboxamides CB1
        receptor modulators for treatment of obesity and other
        diseases)
IT
     Anti-Alzheimer's agents
     Anticonvulsants
     Antidepressants
     Antiobesity agents
     Antiparkinsonian agents
     Antipsychotics
     Anxiolytics
     Cardiovascular agents
     Cognition enhancers
     Immunomodulators
     Nervous system agents
        (preparation of pyrazolecarboxamides CB1 receptor modulators for treatment
        of obesity and other diseases)
IT
     Mental and behavioral disorders
        (psychosis, treatment of; preparation of pyrazolecarboxamides CB1 receptor
        modulators for treatment of obesity and other diseases)
ΙT
     Shock (circulatory collapse)
        (septic, treatment of; preparation of pyrazolecarboxamides CB1 receptor
        modulators for treatment of obesity and other diseases)
TΤ
     Alzheimer's disease
     Anorexia
     Anxiety:
     Cardiovascular system, disease
     Cognitive disorders
     Digestive tract, disease
     Drug dependence
     Endocrine system, disease
     Epilepsy
     Immune disease
     Memory disorders
     Mental and behavioral disorders
     Nervous system, disease
       Obesity
     Parkinson's disease
     Reproduction disorders
     Respiratory system, disease
     Schizophrenia
        (treatment of; preparation of pyrazolecarboxamides CB1 receptor modulators
        for treatment of obesity and other diseases)
IT
     Cannabinoid receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type CB1, modulator; preparation of pyrazolecarboxamides CB1 receptor
        modulators for treatment of obesity and other diseases)
ΙT
                    863639-65-0P
     863639-64-9P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (drug candidate; preparation of pyrazolecarboxamides CB1 receptor modulators
```

```
for treatment of obesity and other diseases)
IT
     863639-38-7P
                    863639-39-8P
                                   863639-40-1P
                                                  863639÷41-2P
                                                                 863639-43-4P
     863639-44-5P
                    863639-46-7P
                                   863639-52-5P
                                                  863639÷56-9P
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                    863639-62-7P
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     863639-68-3P
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                                                                 863639-78-5P
     863639-79-6P
     RL: PAC: (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (drug candidate; preparation of pyrazolecarboxamides CB1 receptor modulators
        for treatment of obesity and other diseases)
IT
     52-52-8, 1-Aminocyclopentanecarboxylic acid
                                                   70-70÷2
                                                             95-92-1, Oxalic
     acid diethyl ester 100-39-0, Benzyl bromide
                                                     109÷61-5, Propyl
                    110-73-6, 2-(Ethylamino)ethanol 141-97-9, Ethyl
     chloroformate
     acetoacetate
                    443-93-6 461-17-6, 1-Iodo-4, 4, 4-trifluorobutane
     554-00-7, 2,4-Dichloroaniline
                                   2213-43-6, 1-Aminopiperidine
                                                                    2386-60-9,
     Butanesulfonyl chloride 2766-74-7, 5-Chlorothiophene-2-sulfonyl chloride
     4319-49-7, 4-Aminomorpholine 10147-36-1, 1-Propanesulfonyl chloride
     10307-18-3
                 13123-92-7, (2,4-Dichlorophenyl) hydrazine 16133-25-8,
     3-Pyridinesulfonyl chloride 16629-19-9, 2-Thiophenesulfonyl chloride
     18742-02-4, 2-(2-Bromoethyl)-1,3-dioxolane
                                                 22795-37-5,
     3-Methylbutane-1-sulfonyl chloride 54696-05-8, 1-(4-
     Benzyloxyphenyl) ethanone
                               63234-70-8, 1-Aminopiperidine hydrochloride
     74784-70-6, 5-(Trifluoromethyl)pyridin-2-amine 178374-78-2
                                                                    212190-25-5
     845866-80-0
                  863639-75-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of pyrazolecarboxamides CB1 receptor modulators for treatment
        of obesity and other diseases)
ΙT
     4495-66÷3P
                  35081-45-9P
                                57696-12-5P
                                              60421-23-0P, Methyl
     1-aminocyclopentanecarboxylate hydrochloride
                                                    152192-95-5P
                                                                   178374-92-0P
                                                                 863639-36-5P
     178374-93-1P
                    502486-92-2P
                                   503270-34-6P
                                                  863639÷35-4P
     863639-37-6P
                    863639-42-3P 863639-47-8P
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                                                                 863639-54-7P
     863639-55-8P
                    863639-57-0P
                                   863639-59-2P
                                                                 863639-70-7P
                                                  863639÷60-5P
     863639-71-8P
                    863639-74-1P
                                   863639-76-3P
                                                  863639÷77-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of pyrazolecarboxamides CB1 receptor modulators for treatment
        of obesity and other diseases)
ΙT
     863639-47-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of pyrazolecarboxamides CB1 receptor modulators for treatment
        of obesity and other diseases)
RN
     863639-47-8 HCAPLUS
     Benzenebutanoic acid, \alpha-acetyl-3,5-difluoro-\beta-methyl-\gamma-
CN
     oxo-4-(phenylmethoxy)-, ethyl ester (9CI) (CA INDEX NAME)
                         0
                    Мe
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 $Ph-CH_2-O$

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L70 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
                        2004:995903 HCAPLUS <<LOGINID::20061121>>
ACCESSION NUMBER:
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DOCUMENT NUMBER: 141:410698

TITLE: Preparation of α -oxoacid-substituted phenols for

the treatment of metabolic disorders

Hodge, Kirvin L.; Sharma, Shalini;

Von Borstel, Reid W.

PATENT ASSIGNEE(S): Wellstat Therapeutics Corporation, USA; Von Borstel,

Reid W.

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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Title compds. I [n = 1-2; m = 0-4; q, p = 0-1; R2 = alkyl; R3 = H, halo; A
     = (un) substituted Ph, cycloalkyl, etc.; R1 = H, alkyl] are prepared For
     instance, 2-oxo-2-[3-(2,6-dimethylbenzyloxy)phenyl]acetic acid (II) is
     prepared by SeO2 oxidation of the corresponding ethanone precursor (prior art).
     II showed a statistically significant decrease in blood glucose and
     triglycerides in obese mice compared to control at 60 mg/Kg. I are useful
     for the treatment of various metabolic disorders, such as insulin
     resistance syndrome, diabetes, hyperlipidemia, fatty liver disease,
     cachexia, obesity, atherosclerosis and arteriosclerosis.
ΙÇ
     ICM A61K
CC
     25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
     Section cross-reference(s): 1, 63
L70 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2004:927013 HCAPLUS <<LOGINID::20061121>>
DOCUMENT NUMBER:
                         141:395291
TITLE:
                         Preparation of benzyloxyphenyl acids and related
                         compounds for the treatment of metabolic disorders
INVENTOR(S):
                         Hodge, Kirvin L.; Kaufman, Robert J.; Lee,
                         Albert; Sharma, Shalini; Von Borstel,
                         Reid W.
PATENT ASSIGNEE(S):
                         Wellstat Therapeutics Corporation, USA
SOURCE:
                         PCT Int. Appl., 42 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                        KIND DATE
     PATENT NO.
                                            APPLICATION NO.
                                                                   DATE
                         ____
                                -----
     WO 2004093806
                         A2
                                20041104
                                            WO 2004-US12142
                                                                   20040420
     WO 2004093806
                         А3
                                20050407
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     CA 2521589
                                20041104
                                            CA 2004-2521589
                          AA
                                                                   20040420
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EP 1618086 A2 20060125 EP 2004-750364 20040420 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, CN 1777576 Α 20060524 CN 2004-80010732 20040420 JP 2006524252 T2 20061026 JP 2006-513151 20040420

> P 20030422 W 20040420

PRIORITY APPLN. INFO.: US 2003-464553P WO 2004-US12142 OTHER SOURCE(S):

MARPAT 141:395291

GΙ

$$z-o$$
 $CH = CH-X-CO-O-R^1$

I

Me
$$CH = CH - CH_2 - CH_2 - CO - OEt$$

Me Me
 Me
 Me
 Me
 Me

AΒ Title compds. I [Z = (CH2)n(NR3)q(CH2)tA; X = (CH2)m; R1 = H, alkyl; R2 =alkyl; R3 = H, halo, alkyl, etc.; n = 1-2; m = 2-3; q = 0-1; t = 0-1; A = 1-2(un) substituted Ph, cycloalkyl, heteroarom, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation of 3-(2,6-dimethylbenzyloxy)benzaldehyde and triphenylethylbutyrate phosphonium bromide afforded claimed benzyloxyphenyl acid ester II in 62% yield. In serum glucose assays in b/db mice, compound II exhibited glucose mg/dL of 651 at 100 mg/kg dosage. Compds. I are claimed useful for the treatment of metabolic disorders, i.e., diabetes, metabolic syndrome X, obesity, etc.

IC ICM A61K

CC 25-18 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds) Section cross-reference(s): 1

L70 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:902090 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER:

141:384282

TITLE:

SOURCE:

Compounds for the treatment of metabolic disorders

INVENTOR(S): Hodge, Kirvin L.; Sharma, Shalini; Von Borstel, Reid W.; Wolpe, Stephen

PATENT ASSIGNEE(S):

Wellstat Therapeutics Corporation, USA

PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|----------------|-----------|---------------------|-----------------|
| | | | | |
| WO 2004091486 | - - | 20041028 | WO 2004-US10799 | 20040408 |
| WO 2004091486 | A3 | 20050120 | | |
| W: AE, AG, | AL, AM, AT | , AU, AZ, | BA, BB, BG, BR, BW, | BY, BZ, CA, CH, |
| CN, CO, | CR, CU, CZ | , DE, DK, | DM, DZ, EC, EE, EG, | ES, FI, GB, GD, |
| GE, GH, | GM, HR, HU | , ID, IL, | IN, IS, JP, KE, KG, | KP, KR, KZ, LC, |
| LK, LR, | LS, LT, LU | , LV, MA, | MD, MG, MK, MN, MW, | MX, MZ, NA, NI, |
| NO, NZ, | OM, PG, PH | , PL, PT, | RO, RU, SC, SD, SE, | SG, SK, SL, SY, |
| TJ, TM, | TN, TR, TT | , TZ, UA, | UG, US, UZ, VC, VN, | YU, ZA, ZM, ZW |
| RW: BW, GH, | GM, KE, LS | , MW, MZ, | SD, SL, SZ, TZ, UG, | ZM, ZW, AM, AZ, |

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     AU 2004229418
                         A1
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                                           NO 2005-4791
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PRIORITY APPLN. INFO.:
                                           US 2003-462960P
                                                               P 20030415
                                           WO 2004-US10799
                                                               W 20040408
OTHER SOURCE(S):
                        MARPAT 141:384282
     Agents such as 4-(3-(2,6-dimethylbenzyloxy)phenyl)-4-hydroxybutanoic acid,
     useful for the treatment of various metabolic disorders, such as insulin
     resistance syndrome, diabetes, hyperlipidemia, fatty liver disease,
     cachexia, obesity, atherosclerosis and arteriosclerosis are disclosed.
     Thus, 4-(3-(2,6-dimethylbenzyloxy)phenyl)-4-(R)-hydroxybutanoic acid was
     prepared by the NaBH4 reduction of 4-(3-(2,6-dimethylbenzyloxy)phenyl)-4-
     oxobutanoic acid. The above compound elicited a significant reduction in blood
     glucose:
IC
     ICM A61K
CC
     63-6 (Pharmaceuticals)
L70
    ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                        2004:718293 HCAPLUS <<LOGINID::20061121>>
DOCUMENT NUMBER:
                        141:236676
                        Compounds for the treatment of metabolic disorders
TITLE:
INVENTOR(S):
                        Hodge, Kirvin L.; Lee, Albert; Sharma,
                         Shalini; Von Borstel, Reid W.
PATENT ASSIGNEE(S):
                        Wellstat Therapeutics Corporation, USA
SOURCE:
                         PCT Int. Appl., 78 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
                        1
PATENT INFORMATION:
     PATENT NO.
                        KIND DATE
                                           APPLICATION NO.
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    WO 2004073611
                        A2
                                           WO 2004-US3718
                               20040902
                                                                  20040209
    WO 2004073611
                        A3
                               20041125
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            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
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A1

AA

A2

20040902

20040902

20051207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

AU 2004-212905

CA 2004-2513092

EP 2004-709467

20040209

20040209

20040209

AU 2004212905

CA 2513092

EP 1601251

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BR 2004007506
                        A
                               20060214
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                        A1
                               20061102
                                           US 2005-531630
                                                                 20050414
     NO 2005003211
                               20051020
                                           NO 2005-3211:
                        Α
                                                                 20050630
PRIORITY APPLN. INFO.:
                                           US 2003-447168P
                                                             P 20030213
                                                             W 20040209
                                           WO 2004-US3718
OTHER SOURCE(S):
                        MARPAT 141:236676
    Agents useful for the treatment of various metabolic disorders, such as
     insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver
     disease, cachexia, obesity, atherosclerosis and arteriosclerosis are
     disclosed. Formula (I) wherein n is 1 or 2; m is 0, 1, 2, 4 or 5; q is 0
     or 1; t is 0 or 1; R2 is alkyl from 1 to 3 carbon atoms; R3 is hydrogen,
     halo, alkyl having from 1 to 3 carbon atoms, or alkoxy having from 1 to 3
     carbon atoms; A is Ph, unsubstituted or substituted by or 1 or 2 groups
     selected from: halo, alkyl having 1 or 2 carbon atoms, perfluoromethyl,
     alkoxy having 1 or 2 carbon atoms, and perfluoromethoxy; or cycloalkyl
     having from 3 to 6 ring carbon atoms wherein the cycloaldyl is
     unsubstituted or one or two ring carbons are independently
     mono-substituted by Me or ethyl; or a 5 or 6 membered heteroarom. ring
     having 1 or 2 ring heteroatoms selected from N, S and O and the
     heteroarom. ring is covalently bound to the remainder of the compds. of
     formula (I) by a ring carbon; and R1 is hydrogen or alkyl having 1 or 2
     carbon atoms. Alternatively, when R1 is hydrogen, the biol. active agent
     can be a pharmaceutically acceptable salt of the compound of Formula (I).
IC
     ICM A61K
CC
     1-10 (Pharmacology)
     Section cross-reference(s): 25
L70 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
                        2004:696360 HCAPLUS <<LOGINID::20061121>>
ACCESSION NUMBER:
DOCUMENT NUMBER:
                        141:225492
TITLE:
                        Preparation of isoxazoles as inhibitors of heat shock
                        proteins
INVENTOR(S):
                        Drysdale, Martin James; Dymock, Brian William; Finch,
                        Harry; Webb, Paul; Mcdonald, Edward; James, Karen
                        Elizabeth; Cheung, Kwai Ming; Mathews, Thomas Peter
PATENT ASSIGNEE(S):
                        Vernalis Cambridge Limited, UK; Cancer Research
                        Technology Ltd; The Institute of Cancer Research; et
                        al.; et al.
SOURCE:
                        PCT Int. Appl., 180 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                        KIND DATE
                                         APPLICATION NO.
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    WO 2004072051
                        A1
                               20040826 WO 2004-GB506
                                                               20040209
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG
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AU 2004210779

A1

20040826

AU 2004-210779

20040209

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CA 2515726
                          AΑ
                                20040826
                                             CA 2004-2515726
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     EP 1611112
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     CN 1771235
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     JP 2006517572
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                                20061026
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PRIORITY APPLN. INFO.:
                                             GB 2003-3105
                                                                 A 20030211
                                             GB 2003-6560
                                                                 A 20030321
                                             GB 2003-13751
                                                                 A 20030613
                                             WO 2004-GB506
                                                                 W 20040209
OTHER SOURCE(S):
                         MARPAT 141:225492
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$$R^1$$
 R^2
 R^3
 R^3
 R^3
 R^3
 R^3
 R^3
 R^3

ΑB Title compds. [I, II; R1 = Ar1(Alk1)p(Z)r(Alk2)sQ; Ar1 = (substituted)aryl, heteroaryl; Alkl, Alk2 = (substituted) alkylene, alkenylene; p, r, s = 0, 1; Z = 0, S, CO, CS, SO2, CO2, CONRA, CSNRA, SO2NRA, NRACO, NRASO2, NRA; RA = H, alkyl; Q = H, (substituted) carbocyclyl, heterocyclyl; R2 = Ar1(Alk1)p(Z)r(Alk2)sQ, carboxamide, carboxyclyl, heterocyclyl optionally substituted by (Alk1)pZr(Alk2)sQ; R3 = H, (substituted) cycloalkyl, cycloalkenyl, alkyl, alkenyl, alkynyl, carboxyl, carboxamide, carboxyl ester], were prepared Thus, NH2OH.HCl and 7-hydroxy-3-(4-methoxyphenyl)-2methylchromen-4-one (preparation given) were refluxed 4 h in pyridine to give 4-[4-(4-methoxyphenyl)-3-methylisoxazol-5-yl]benzene-1,3-diol. The latter in the Malachite Green ATPase assay inhibited HSP90 with IC50 <50 μM.

IC ICM C07D261-08

C07D413-04; C07D413-10; C07D417-04; C07D261-10; C07D495-04; A61P035-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom)) Section cross-reference(s): 1, 63

ITEye, disease

> (diabetic retinopathy, treatment; preparation of isoxazoles as inhibitors of heat shock proteins)

ΙT Autoimmune disease

> (insulin-dependent diabetes mellitus, treatment; preparation of isoxazoles as inhibitors of heat shock proteins)

ΙT Diabetes mellitus

> (insulin-dependent, treatment; preparation of isoxazoles as inhibitors of heat shock proteins)

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IT
     487-49-0P
                 2284-30-2P
                              13004-42-7P
                                            19337-03-2P
                                                          22877-01-6P
     23504-03-2P
                   29048-54-2P
                                 90110-32-0P
                                               103620-87÷7P 130307-08-3P
     140660-31-7P
                    328018-52-6P
                                   536974-86-4P:
                                                  558645+35-5P
                                                                  705963-54-8P
     747412-81-3P
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                                                  747413÷00-9P
     747413-03-2P
                    747413-04-3P
                                   747413-05-4P
                                                  747413-06-5P
     747413-07-6P
                    747413-12-3P
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747413-72-5P 747413-69-0P 747413-70-3P 747413-71-4P 747413-73-6P 747413-74-7P 747413-75-8P 747414-06-8P 747414-07-9P 747414-11-5P 747414-08-0P 747414-09-1P 747414-10-4P 747414-12-6P 747414-16-0P 747414-17-1P 747414-18-2P 747414-19-3P 747414-20-6P 747414-21-7P 747414-22-8P 747414-23-9P 747414-24-0P 747414-48-8P 747414-49-9P 747414-50-2P 747414-51-3P 747414-52-4P 747414-53-5P 747414-55-7P 747414-56-8P 747414-57-9P 747414-62-6P 747414-63-7P 747414-65-9P 747414-69-3P 747414-64-8P 747414-66-0P 747414-67-1P 747414-71-7P 747414-72-8P 747414-70-6P 747414÷73-9P 747414-74-0P 747414-76-2P 747414-78-4P 747414÷79-5P 747414-80-8P 747414-84-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoxazoles as inhibitors of heat shock proteins)

IT 747413-03-2P 747413-69-0P 747414-70-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoxazoles as inhibitors of heat shock proteins)

RN 747413-03-2 HCAPLUS

CN 2-Butenoic acid, 4-[5-chloro-2,4-bis(phenylmethoxy)phenyl]-2-hydroxy-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

$$C1$$
 $C-CH = C-C-OEt$ $C-CH_2-Ph$

RN 747413-69-0 HCAPLUS

CN Benzenebutanoic acid, 5-bromo- α , γ -dioxo-2,4-bis(phenylmethoxy)-, ethyl ester (9CI) (CA INDEX NAME)

RN 747414-70-6 HCAPLUS

CN Benzenebutanoic acid, 3-chloro- α , γ -dioxo-4-(phenylmethoxy)- β -(triphenylphosphoranylidene)-, ethyl ester (9CI) (CA INDEX NAME)

L70 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2002:964135 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER:

138:24543

TITLE:

Preparation of benzyloxyphenyloxobutyrates and related

compounds for the treatment of metabolic disorders INVENTOR(S): Sharma, Shalini; Von Borstel, Reid

W.; Hodge, Kirvin L.

PATENT ASSIGNEE(S):

Wellstat Therapeutics Corporation, USA; Bamat, Michael

Κ.

SOURCE:

PCT Int. Appl., 242 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002100341 WO 2002100341 | A2 A3 | 20021219 | WO 2002-US18388 | 20020612 |
| W: AE, AG, CO, CR, GM, HR, LS, LT, PL, PT, UA, UG, RW: GH, GM, KG, KZ, | AL, AM, AT, CU, CZ, DE, HU, ID, IL, LU, LV, MA, RO, RU, SD, US, UZ, VN, KE, LS, MW, MD, RU, TJ, | AU, AZ, DK, DM, IN, IS, MD, MG, SE, SG, YU, ZA, MZ, SD, TM, AT, | BA, BB, BG, BR, BY, DZ, EC, EE, ES, FI, JP, KE, KG, KP, KR, MK, MN, MW, MX, MZ, SI, SK, SL, TJ, TM, | GB, GD, GE, GH, KZ, LC, LK, LR, NO, NZ, OM, PH, TN, TR, TT, TZ, ZW, AM, AZ, BY, ES, FI, FR, GB, |
| GN, GQ, CA 2450221 | GW, ML, MR, | NE, SN, 20021219 | | 20020612 |
| US 7101910 | В2 | 20060905 | EP 2002-744271 | |
| R: AT, BE, IE, FI, | CH, DE, DK, CY, TR | , ES, FR, | GB, GR, IT, LI, LU, | |
| JP 2005501012 CN 1608055 BR 2002010383 | T2 A | 20050113 20050420 20060404 | JP 2003-503168 CN 2002-811881 BR 2002-10383 | 20020612 |
| US 2004077896 | A1 | 20040422 20050802 | US 2003-684644 | 20031014 |
| | B2 | 20040513 20060509 | US 2003-684735 | |
| US 6946491 US 2004097585 | B2 A1 | 20040513 20050920 20040520 | US 2003-685183 US 2003-684730 | |
| US 6916848 | B2 | 20050712 | | |

| : | | | | | | |
|------------------------|-----|----------|----|--------------|----|----------|
| US 2004236100 | A1 | 20041125 | US | 2003-684660 | | 20031014 |
| US 6858602 | В2 | 20050222 | | | | |
| US 2004267025 | A1 | 20041230 | US | 2003-684740 | | 20031014 |
| US 7045541 | В2 | 20060516 | | | | |
| ZA 2003009627 | Α | 20050617 | zA | 2003-9627 | | 20031211 |
| US 2004242692 | A'1 | 20041202 | US | 2004-865088 | | 20040610 |
| US 2005004115 | A1 | 20050106 | US | 2004-892950 | | 20040716 |
| US 7012071 | В2 | 20060314 | | | | |
| US 2005090555 | A1 | 20050428 | US | 2004-5449 | | 20041206 |
| US 2005256333 | A1 | 20051117 | US | 2005-481042 | | 20050114 |
| PRIORITY APPLN. INFO.: | | | US | 2001-297282P | P | 20010612 |
| | | | US | 2002-167839 | A3 | 20020612 |
| : | | | WO | 2002-US18388 | W | 20020612 |
| : : | | | US | 2003-685183 | A3 | 20031014 |
| : | | | US | 2004-865088 | A1 | 20040610 |

OTHER SOURCE(S):

MARPAT 138:24543

GI

$$A(CH_2)_p(NR^5)_q(CH_2)_nO$$
(CH₂)_mCOXCOQ I

AΒ Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = alkylH, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 = Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2, Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other = H, alkyl], were prepared Thus, 4-(2-fluorobenzyloxy) acetophenone (preparation given) in THF and DMPU was treated with a solution of Li bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu bromoacetate was added followed by stirring for an addnl. 10 min and warming to room temperature for 4 h to give tert-Bu 4-[4-(2fluorobenzyloxy)phenyl]-4-oxobutyrate. The latter was stirred with CF3CO2H in CH2C12 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric acid. Tested I showed antidiabetic activity in a variety of tests. I are useful in treatment of various metabolic disorders such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis.

IC ICM A61K

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds) Section cross-reference(s): 1, 27, 28

L70 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:676588 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER: 135:221312

TITLE:

Therapeutic uses of PPAR mediators as ABC-1 expression

modulators, and preparation thereof

Jaye, Michael; Duverger, Nicolas; Searfoss, George; INVENTOR(S):

Minnich, Anne

PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany

PCT Int. Appl., 176 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

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PATENT INFORMATION:

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PATENT NO.
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    WO 2001066098
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                                           WO 2001-EP2482
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    WO 2001066098
                        А3
                               20020404
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            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
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    US 2003220373)
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                                           US 2002-237578
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PRIORITY APPLN. INFO.:
                                           US 2000-188323P
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                                           GB 2000-13589
                                                             A 20000606
                                           WO 2001-EP2482
                                                              W 20010306
OTHER SOURCE(S):
                        MARPAT 135:221312
    The invention discloses the use of PPAR mediators, and their
    pharmaceutical compns., as ATP binding cassette transporter 1 (ABC-1)
    expression modulators, wherein the PPAR ligand receptor agonists of the
     invention are useful as inducers of ABC-1 expression. Preparation of compds.
    of the invention is included. Also disclosed are methods for treating
    e.g. low levels of HDL.
IC
    ICM A61K031-00
CC
    1-10 (Pharmacology)
    Section cross-reference(s): 27, 28, 63
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     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (PPAR mediators as ABC-1 expression modulators, preparation, and therapeutic
        use)
IT
     223772-45-0P 223772-46-1P
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (PPAR mediators as ABC-1 expression modulators, preparation, and therapeutic
        use)
RN
     223772-45-0 HCAPLUS
CN
     Benzenebutanoic acid, 3-fluoro-γ-oxo-4-[[3-(2-
     quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX NAME)
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$$\begin{array}{c} O \\ C - CH_2 - CH_2 - CO_2H \\ \end{array}$$

RN 223772-46-1 HCAPLUS CN Benzenebutanoic acid, 3-fluoro-y-oxo-4-[[4-(2quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX NAME)

$$CH_2-O$$
 $CH_2-CH_2-CH_2-CO_2H$

L70 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2000:772613 HCAPLUS <<LOGINID::20061121>> DOCUMENT NUMBER:

133:335164

TITLE: Tri-aryl acid derivatives as PPAR receptor ligands

INVENTOR(S):

Jayyosi, Zaid; McGeehan, Gerard M.; Kelley, Michael F.; Labaudiniere, Richard F.; Zhang, Litao; Caulfield, Thomas J.; Minnich, Anne; Bobko, Mark; Morris, Robert; Groneberg, Robert D.; Mcgarry, Daniel G.

PATENT ASSIGNEE(S):

SOURCE:

Aventis Pharmaceuticals Products Inc., USA

PCT Int. Appl., 257 pp.

DOCUMENT TYPE:

LANGUAGE:

CODEN: PIXXD2 Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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| | CG, | CI, | CM, | GA, | GN, | GW, | | | | | | | | | | | |
| CA 237 | 1308 | | | AA | | 2000 | 1102 | | CA | 20 | 000- | 2371 | 308 | | 2 | 0000 | 428 |
| EP 117 | / † / p | | | AI | | 2002 | 0206 | | EΡ | 20 | 000- | 9302 | 10 | | 2 | 0000 | 428 |
| EP 117 | 7176 | | | В1 | | 2006 | 0419 | | | • | | | 1 | | | | |
| R: | AT, | ΒE, | CH, | DE, | DK, | ES, | FR, | GB, | GF | ₹, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
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| BR 200 | 00101 | 26 | | Α | | 2002 | 0226 | | BR | 20 | 000- | 1012 | 6 | | 2 | 0000 | 428 |
| HU 200 | 20099 | 7 | | A2 | | 2002 | 0729 | | HU | 20 | 002- | 997 | | | 2 | 0000 | |
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| PT 117 | | | | T | | 2006 | | | PT | 20 | 000- | 9302 | 10 | | 2 | 0000 | 428 |
| US 700 | 5440 | | | В1 | | 2006 | | | US | 20 | 000- | 7244 | 96 | | 2 | 0001 0011 0011 | 128 |
| ZA 200 | | 00 | | Α | | 2003 | | | ZA | 20 | 01- | 8800 | į | | 2 | 0011 | 024 |
| NO 200 | | | | Α | | 2001 | | | NO | 20 | 01- | 5226 | - | | 2 | 0011 | 025 |
| HR 200 | | | | | | | | | HR | 20 | 01- | 793 | | | 2 | 0011 | |
| HK 104 | | | | A1 | | 2005 | 0520 | | | | | | 2 5 | | | 0021 | |
| RIORITY AP | PLN. | INFO | . : / | | | | | | US | 19 | 99- | 1314 | 54P | | P 1 | 9990 | 428 |
| | _ ; | | | | | | | | WO | 20 | 000- | JS11 | 490 | 1 | ₩ 2 | 0000 | 428 |
| THER SOURC | E(S): | | | MARI | PAT | 133: | 3351 | 64 | | | | | : | | | | |
| I | | | | | | | | | | : | | | } | | | | |

$$Ar1 \xrightarrow{R1} A \xrightarrow{R3} Ar2 \xrightarrow{R5} R7 \xrightarrow{R9} R11$$

$$Ar1 \xrightarrow{R1} A \xrightarrow{R1} Ar2 \xrightarrow{R1} R6 \xrightarrow{R8} Ar3 \xrightarrow{R9} D \xrightarrow{R1} E - Z$$

$$R2 \xrightarrow{R4} R4 \xrightarrow{R6} R8 \xrightarrow{R8} R10 \xrightarrow{R10} R12 \xrightarrow{R12} I$$

AB This invention is directed to triaryl acid derivs. I and their salts, N-oxides, hydrates, solvates, and pharmaceutical compns. [wherein: Ar1, Ar2, Ar3 = aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkemyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl; A = bond, O, S, SO, SO2, CO, (un) substituted NH, NHCO, CONH, NHCONH, CH:N, etc.; B = bond, O, S, SO, SO2, C.tplbond.C, CO, (un) substituted NH, NHCO, or CONH; D = bond, O; S, C.tplbond.C, CO, (un)substituted NH, NHCO, or CONH; E = bond, CH2CH2; Z = (un) substituted CO2H, CHO, cyclo-imide, cyano, sulfonylaminocarbonyl, sulfonylamino, carbamoyl, tetrazolyl, etc.; R1, R3, R5, R7, R9, R11 = H, halo, alkyl, CO2H, alkoxycarbonyl, aralkyl; R2, R4, R6, R8, R10, R12 = (CH2)0-3X (where X = H or various substituents); $n1 = \frac{1}{2}$ 0-4; m1 = 0-4; n = 0-4; m = 0-5; p = 0-4; q = 0-6; with numerous provisos]. The compds. are PPAR receptor ligands, useful as agonists or antagonists thereof (no data). For instance, 2,6-dimethylbenzoic acid underwent a sequence of: (1) Me esterification, (2) benzylic monobromination, (3) etherification with 3-(quinolin-2-ylmethoxy)phenol, and (4) alkaline hydrolysis with NaOH in aqueous EtOH, to give title compound II.

IC ICM C07D215-14

ICS A61K031-33; A61K031-19; A61P043-00; C07D401-12; C07D401-14; C07D215-18; C07D405-12; C07D263-32; C07D213-30; C07D241-42; C07D277-24; C07D261-08; C07D271-06; C07D277-64

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Diabetes mellitus

(non-insulin-dependent, treatment of; preparation of tri-aryl acid derivs.
as PPAR receptor ligands)

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223772-45-0P 223772-46-1P
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(Uses)
   (preparation of tri-aryl acid derivs. as PPAR receptor ligands)
223772-45-0 HCAPLUS
Benzenebutanoic acid, 3-fluoro-\gamma-oxo-4-[[3-(2-
quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX:NAME)
```

$$\begin{array}{c} O \\ C - CH_2 - CH_2 - CO_2H \end{array}$$

ΙT

RN

CN

RN 223772-46-1 HCAPLUS

CN Benzenebutanoic acid, 3-fluoro-γ-oxo-4-[[4-(2quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX NAME)

$$CH_2-O$$
 $CH_2-CH_2-CH_2-CO_2H$

RETABLE

| Referenced Author | Year VOL | PG I | Referenced Work | Referenced |
|-------------------------|---------------|-----------|-----------------|------------|
| (RAU) | (RPY) (RVL) | (RPG) | (RWK) | File |
| | +====+==== | +=====+== | | ==+====== |
| Ciba-Geigy Ag | 1995 | E | P 0643045 A | HCAPLUS |
| Dr Reddy'S Research Fou | 1999 | WC | 9908501 A | HCAPLUS |
| Glaxo Group Ltd | 1997 | W | 9731907 A | HCAPLUS |
| Laboratorios Menarini S | 1997 | WC | 9724331 A | HCAPLUS |
| Leo Pharmaceutical Prod | 1989 | W(| 0 8905294 A | HCAPLUS |
| Merck & Co Inc | 1997 | W(| 9728149 A | HCAPLUS |
| Merck & Co Inc | 1997 | WC | 9727857 A | HCAPLUS |
| Merck & Co Inc | 1998 | W(| 9827974 A | HCAPLUS |
| Ono Pharmaceutical Co I | 1999 | WC | 9907357 A | HCAPLUS |
| RhOne-Poulenc Rorer Pha | 1999 | WC | 0 9920275 A | HCAPLUS |
| Rorer International Ove | 1989 | W | 0 8904303 A | HCAPLUS |
| Rorer International Ove | 1989 | W | 0 8912629 A | HCAPLUS |
| The Upjohn Company | 1992 | W | 9222533 A | HCAPLUS |

L70 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:282096 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER: 130:320864

TITLE: PPAR- γ -binding quinoline derivatives, their

preparation, and their therapeutic use

INVENTOR(S): Jayyosi, Zaid; McGeehan, Gerard M.; Kelley, Michael F.

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

LANGUAGE: En FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

| PATENT NO. | | KIND | DATE | APPLICATION NO. | DATE |
|------------|---------|--------|-----------|---------------------|-----------------|
| WO 9920275 | | A1 | 19990429 | WO 1998-US21947 | 19981016 |
| W: AL, | AM, AT, | AU, AZ | , BA, BB, | BG, BR, BY, CA, CN, | CU, CZ, DE, DK, |
| EE, | ES, FI, | GB, GE | , GH, HU, | IL, IS, JP, KE, KG, | KP, KR, KZ, LC, |
| LK, | LR, LS, | LT, LU | , LV, MD, | MG, MK, MN, MW, MX, | NO, NZ, PL, PT, |
| | | | | SL, TJ, TM, TR, TT, | |
| VN, | YU, ZW | | | , | |
| RW: GH, | GM, KE, | LS, MW | , SD, SZ, | UG, ZW, AT, BE, CH, | CY, DE, DK, ES, |
| | | | | MC, NL, PT, SE, BF, | |

GI

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CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              CA 1998-2306825
     CA 2306825
                           AA
                                 19990429
                                                                      19981016
     AU 9896961
                           A1
                                 19990510
                                              AU 1998-96961
                                                                      19981016
     ZA 9809465
                           Α
                                 20000417
                                              ZA 1998-9465
                                                                      19981016
     EP 1030665
                           A1
                                 20000830
                                              EP 1998-951075
                                                                      19981016
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, FI, RO
     BR 9814087
                                 20001003
                                              BR 1998-14087
                                                                      19981016
                           Α
     HU 200101022
                           Α2
                                 20011028
                                              HU 2001-1022
                                                                      19981016
     JP 2001520193
                           T2
                                 20011030
                                              JP 2000-516672
                                                                      19981016
     US 6376512
                           В1
                                 20020423
                                              US 2000-490897
                                                                      20000127
     NO 2000001962
                           Α
                                 20000616
                                              NO 2000-1962
                                                                      20000414
     BG 104432
                           Α
                                 20001229
                                              BG 2000-104432
                                                                      20000515
PRIORITY APPLN. INFO.:
                                              US 1997-62318P
                                                                   Ρ
                                                                      19971017
                                              US 1997-65902P
                                                                   Ρ
                                                                      19971117
                                              WO 1998-US21947
                                                                      19981016
OTHER SOURCE(S):
                          MARPAT 130:320864
```

$$\left\langle \begin{array}{c} (R)_{n} \\ \vdots \\ (C)_{e} \end{array} \right\rangle = D - \left(\begin{array}{c} R^{2} \\ (C)_{f} \end{array} \right) = E - Z$$

AB A method for mediating the activity of PPAR- γ receptor comprises contacting the PPAR- γ receptor with I [A = O, S, (R1)C=C(R1), bond; B = O, S, SO, SO2, NR1, bond; D = O, S, NR1, (R1)C=C(R1), bond; E = bond; a = 0-2; b = 0, 1; c = 0-4; d = 0-5; e = 0-4; f = 0-5; n = 0-2; R = H; R' = H; R1 = H; R2 = (CH2)qX, or two vicinal R2 taken together with the carbon atoms through which the two vicinal R2 are linked form cycloalkylene, etc.; q = 0-3; X = H]. Preparation of I is described. The compds. may be used to treat cardiovascular conditions, diabetes, hyperlipidemia, hypertension, eating disorders, etc.

Ι

IC ICM A61K031-47

ICS A61K031-38; A61K031-35; A61K031-155; A61K031-18

CC 1-12 (Pharmacology)

Section cross-reference(s): 27, 28

IΤ 114497-47-1P 123225-56-9P 123225-57-0P 123225÷58-1P 123225-59-2P 123225-60-5P 123225-61-6P 123225-63-8P 123225+64-9P 123225-69-4P 123225-71-8P 123225-72-9P 123225-76-3P: 123225÷82-1P 123225-94-5P 123225-95-6P 123225-96-7P 123225-98-9P 123225÷99-0P 123226-00-6P 123226-01-7P 123226-03-9P 123226-04-0P 123226÷05-1P 123226-06-2P 123226-07-3P 123226-08-4P 123226-09-5P 123226÷10-8P 123226-11-9P 123226-13-1P 123226-14-2P 123226-15-3P 123226+16-4P 123226-17-5P IT

RN

CN

123226-19-7P 123226-20-0P 123226-21-1P 123226+25-5P 123226-27-7P 123247-23-4P 123247-25-6P 123247-27-8P 123247-28-9P 123692-25-1P 123692-29-5P 123692-37-5P 123692-38-6P 123692÷39-7P 123791-11-7P 123791-15-1P 124993-46-0P 124993-48-2P 128760÷62-3P 128760-70-3P 128760-73-6P 129649-40-7P 223772-08-5P 223772-12-1P 223772-14-3P 223772-15-4P 223772-18-7P 223772-26-7P 223772-42-7P 223772-43-8P 223772-44-9P **223772-45-0P 223772-46-1P** 223772-47-2P 223772-48-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PPAR- γ -binding quinoline derivative preparation and therapeutic use) 223772-45-0P 223772-46-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PPAR- γ -binding quinoline derivative preparation and therapeutic use) 223772-45-0 HCAPLUS

Benzenebutanoic acid, 3-fluoro-γ-oxo-4-[[3-(2-quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX NAME)

$$CH_2 - O$$
 $CH_2 - CH_2 - CH_2 - CO_2H$

RN 223772-46-1 HCAPLUS

CN Benzenebutanoic acid, 3-fluoro-γ-oxo-4-[[4-(2quinolinylmethoxy)phenyl]methoxy]- (9CI) (CA INDEX NAME)

$$CH_2-O$$
 $CH_2-CH_2-CH_2-CO_2H$

RETABLE

| Referenced Author (RAÜ) | Year VOL (RPY) (RVL |) (RPG) | Referenced Work (RWK) | Referenced File |
|--|---------------------------|-----------|-----------------------|----------------------|
| Asahi Glass Company Lt Merrell Dow Pharmaceut | d 1996 | i i E | P 0709377 A1 | HCAPLUS HCAPLUS |
| Sterne | 11965 | | S 3174901 A | HCAPLUS |

L70 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:497460 HCAPLUS <<LOGINID::20061121>>

DOCUMENT NUMBER: 113:97460

TITLE: Preparation of quinoline derivatives useful as

lipoxygenase inhibitors and/or leukotriene antagonists INVENTOR(S):

Huang, Fu Chi; Galemmo, Robert Anthony, Jr.; Campbell,

Henry Flud

PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA

SOURCE: Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND . | DATE | APPLICATION NO. | DATE |
|-------------------------|---------|----------------------|----------------------------------|----------------------|
| EP 348155 EP 348155 | A1 | 19891227 | EP 1989-306232 | 19890620 |
| R: DE, ES, FR, | • | 19990512 | | |
| US 4920131 EP 784052 | A A1 | 19900424 19970716 | US 1988-209428 EP 1997-200638 | 19880621 19890620 |
| EP 784052 | B1 | 20040901 | БР 1997-200036 | 19090020 |
| R: DE, ES, FR, | GB, IT | | | |
| US 5059610 | А | 19911022 | US 1990-477896 | 19900420 |
| PRIORITY APPLN. INFO.: | | | US 1988-209428 | A 19880621 |
| | | | US 1987-116420 | A2 19871103 |
| : | | | US 1987-116428 | A2 19871103 |
| | | | US 1987-116597 | A2 19871103 |
| | | | WO 1988-US3897 | W 19881101 |
| | | | EP 1989-306232 | A3 19890620 |

OTHER SOURCE(S): MARPAT 113:97460 GΙ

$$\begin{cases} R & R \\ C & C \\ R & R \end{cases}$$

Ι

```
AB
       Title compds. I [A = O, S; B = bond, O, S, SO, SO2, NR1, CO, NR1CO, CONR1,
       CR1:CR1; D = O, S, NR1, CR1:CR1, bond; E = bond, CR1:CR1; a = 0-2; b = 0
       0-1; c = 0-4; d = 0-5, e = 0-4; f = 0-5; n = 0-2; R2 = H, alkyl, OH,
       alkoxy, CO2H, carbalkoxy, halo NO2, haloalkyl, cyano, acyl; R3 = H, OH,
       alkoxy, halo, etc.; RI = H, alkyl, aralkyl; R = (CH2)xX, O(CH2)xX,
       S(CH2) \times X, NR1(CH2) \times X; x = 0-3; X = H, alkyl, alkenyl, aryl, alkoxy, amino,
       cyano, tetrazolyl, CO2R, etc.; (R)2 = (CH2)y with y = 1-4; RR1 = (CH2)z
       with z = 2-5; (R1)2, RR1 = CHR1; Z = CO2R1, cyano, CONHSO2R4 with R4 = H,
       alkyl, Ph, etc.; CON(R1)2, OR1, (un)substituted tetrazolyl] were prepared as
       antiinflammatory and antiallergic agents (no data). Thus, condensation of
       o-cresol with MeCHBr Co2Et and bromination of the product with NBS gave
       2-(BrCH2)C6H4 OCHMeCO2Et, which underwent condensation with
       3-(2-quinolinylmethoxy) phenol and basic hydrolysis to give quinoline
       derivative II. Several addnl. prepns. and numerous I are given.
 IC
       ICM C07D215-14
       ICS C07D215-18; C07D401-12; A61K031-47
       27-17 (Heterocyclic Compounds (One Hetero Atom))
 CC
       Section cross-reference(s): 1
 ΙT
       120128-20-3P
                      123247-27-8P
                                      128760-39-4P
                                                     128760-40-7P
                                                                    128760-41-8P
       128760-42-9P
                      128760-43-0P
                                      128760-44-1P
                                                     128760-45-2P
                                                                    128760-46-3P
       128760-47-4P
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                                      128760-49-6P
                                                     128760-50-9P
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                                                                     128760-71-4P
       128760-72-5P
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                                                                    128760-76-9P
       128760-86-1P
                      128760-87-2P 128784-91-8P
                                                  128784-92-9P
       128805-38-9P
       RL: SPN: (Synthetic preparation); PREP (Preparation)
          (preparation of, as antiallergic and antiinflammatory agent)
  ΙT
       128784-91-8P
       RL: SPN (Synthetic preparation); PREP (Preparation)
          (preparation of, as antiallergic and antiinflammatory agent)
 RN
       128784-91-8 HCAPLUS
       Benzenebutanoic acid, 3-fluoro-γ-hydroxy-4-[[4-(2-
 CN
       quinolinylmethoxy)phenyl]methoxy]-, methyl ester (9CI)
                                                               (CA INDEX NAME)
                                                           0
                                                  CH2-CH2-
▶ L70 ANSWER 14 OF 15
                        HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER:
                           1980:471315 HCAPLUS <<LOGINID::20061121>>
```

2-(Substituted benzoyl) propionic acids

Hisamitsu Pharmaceutical Co., Inc., Japan

Masayoshi; Ide, Hiroyuki

Jpn. Kokai Tokkyo Koho, 3 pp.

Noda, Kanji; Nakagawa, Akira; Hirano, Munehiko; Tsuji,

93:71315

SOURCE:

TITLE:

DOCUMENT NUMBER:

PATENT ASSIGNEE(S):

INVENTOR(S):

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|------------------------|------|----------|-----------------|---|----------|
| | | | | | |
| JP 55015460 | A2 | 19800202 | JP 1978-89591 | | 19780720 |
| PRIORITY APPLN. INFO.: | | | JP 1978-89591 | Α | 19780720 |
| CT : | | | : | | |

$$R^2$$
 R^1 $COCH_2CH_2CO_2R$

AB Seven I (R = H; R1 = Me2CH, H; R2 = H, NO2, C1; R3 = Me2CH, EtO, cyclopropylmethoxy, allyloxy, etc.), having central-depressant, antiinflammatory, PCA-inhibitory and immunosuppressant activities (no data), were prepared by reacting succinic anhydride (II) with C6H6 derivs., or by reacting I (R = Et, R3 = OH) with R3Br (R3 = cyclopropylmethyl), followed by hydrolysis. Thus, m-(Me2CH)2C6H4 16.2 was added dropwise to II 10 and AlCl3 26.7 g in ClCH2CH2Cl with cooling, and the mixture was stirred 10 h at room temperature to give I (R = R2 = H, R1 = R3 = CHMe2).

IC C07C059÷76; C07C079-46; C07C101-44

CC 25-18 (Noncondensed Aromatic Compounds)

IT 74362-69-9P 74362-70-2P 74362-71-3P 74362-72-4P **74362-73-5P**

74362-74-6P 74391-08-5P

IT 74362-73-5P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 74362-73-5 HCAPLUS

CN Benzenebutanoic acid, 3-chloro-γ-oxo-4-(phenylmethoxy)- (9CI) (CA TNDEX NAME)

L53 ANSWER 1 OF 1 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN AN.S DCR-905973
DCSE 905973-0-0-0
CN.S 4-(4-Benzyloxy-3-chloro-phenyl)-4-oxo-butyric acid

MF C17 H15 C1 O4 SMF C17 H15 C1 O4 *1; TOTAL *1; TYPE *1 MW 318.7597 SDCN RAECKI

=> d all abeq tech 169 tot

ANSWER 1 OF 1 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN ΑN 2004-411395 [38] WPIX <<LOGINID::20061121>> DNC C2004-154379 [38] ΤI Use of oxoalkanoates in the manufacture of a medicament for treatment of metabolic disorders e.g. insulin resistance syndrome and diabetes DC IN HODGE K L; SHARMA S; VON BORSTEL R W; WOLPE S D PA (WELL-N) WELLSTAT THERAPEUTICS CORP; (HODG-I) HODGE K L; (SHAR-I) SHARMA S; (VBOR-I) VON BORSTEL R W; (WOLP-I) WOLPE S D CYC 105 PI WO 2004041165 A2 20040521 (200438)* EN 22[0] A61K000-00 AU 2003286728 A1 20040607 (200469) EN EP 1556085 A2 20050727 (200549) A61K047-00 US 20060035970 A1 20060216 (200614) ΕN JP 2006507303 W 20060302 (200621) JA AU 2003286728 A8 20051110 (200634) EN A61K047-00 ADT WO 2004041165 A2 WO 2003-US34185 20031028; US 20060035970 A1 Provisional US 2002+423253P 20021101; AU 2003286728 A1 AU 2003-286728 20031028; EP 1556085 A2 EP 2003-777939 20031028; EP 1556085 A2 WO 2003-US34185 20031028; US 20060035970 A1 WO 2003-US34185 20031028; JP 2006507303 W WO 2003-US34185 20031028; JP 2006507303 W JP 2004-550151 20031028; US 20060035970 A1 US 2005-532690 20050426; AU 2003286728 A8 AU 2003-286728

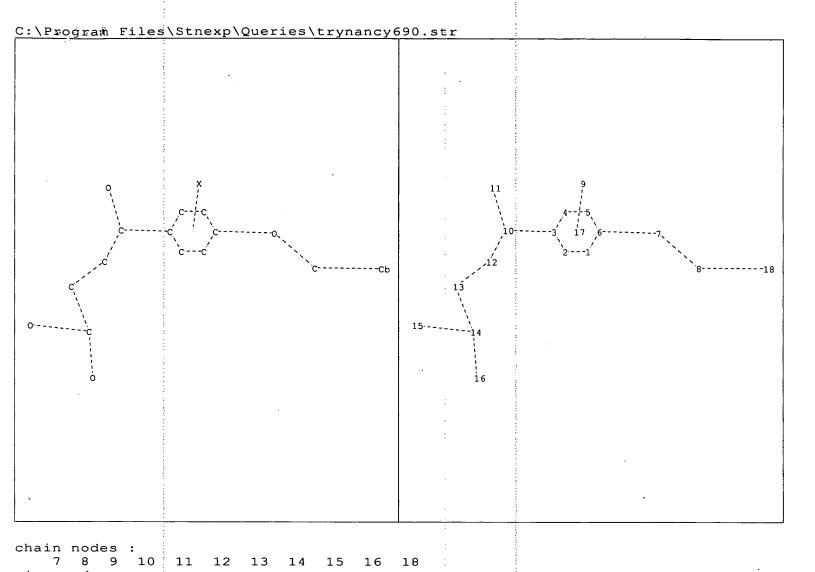
FDT AU 2003286728 A1 Based on WO 2004041165 A; EP 1556085 A2 Based on WO 2004041165 A; JP 2006507303 W Based on WO 2004041165 A; AU 2003286728 A8 Based on WO 2004041165 A

PRAI US 2002-423253P 20021101

20031028

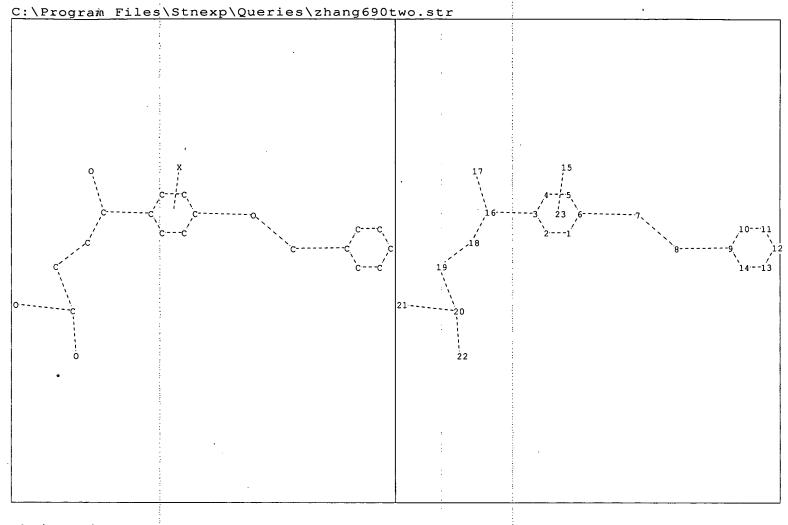
US 2005÷532690 20050426

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ICM A61K005-; A61K047-00
IC
IPCI A61K0031-185 [I,C]; A61K0031-192 [I,A]; A61K0031-21 [I,C]; A61K0031-235
     [I,A]; A61K0031-185 [I,C]; A61K0031-192 [I,A]; A61K0031-21 [I,C];
     A61K0031-216 [I,A]; A61P0001-00 [I,C]; A61P0001-16 [I,A]; A61P0013-00
     [I,C]; A61P0013-12 [I,A]; A61P0017-00 [I,C]; A61P0017-02 [I,A];
     A61P0025-00 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0027-12
     [I,A]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-06 [I,A];
     A61P0003-10 [I,A]; A61P0009-00 [I,C]; A61P0009-10 [I,A]; A61P0009-12 [I,A]
AB
     WO 2004041165 A2 UPAB: 20060121
      NOVELTY - Treatment of metabolic disorders involves administration of an
     agent.
            DETAILED DESCRIPTION - Treatment of metabolic disorders involves
     administration of an agent selected from:
            (1) 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid;
            (2) methyl 4-(4-benzyloxy-2-methoxyphenyl)-4-oxobutanoate;
            (3) ethyl 4-(4-cyclohexylmethoxyphenyl)-4-oxobutanoate;
            (4) 4-(3-chloro-4-cyclopropylmethoxyphenyl)-4-oxobutanoic acid;
            (5) ethyl 3-(4-benzyloxyphenyl)-3-oxopropanoate;
            (6) ethyl 3-(3-benzyloxyphenyl)-3-oxopropanoate;
            (7) ethyl 3-(2-benzyloxyphenyl)-3-oxopropanoate;
            (8) methyl 3-(3-(2,6-dichlorobenzyloxy)phenyl)-3-oxopropanoate;
            (9) ethyl 3-(4-(4-chlorobenzyloxy)phenyl)-3-oxopropanoate;
            (10) ethyl 3-(3-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;
            (11) ethyl 3-(2-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;
            (12) ethyl 3-(2-(2-methoxybenzyloxy)phenyl)-3-oxopropanoate;
            (13) ethyl 3-(2-(3-methoxybenzyloxy)phenyl)-3-oxopropanoate;
            (14) ethyl 3-(4-benzyloxy-3-chlorophenyl)-3-oxopropanoate;
            (15) ethyl 3-(4-benzyloxy-3-methoxyphenyl)-3-oxopropanoate; or
            (16) ethyl 3-(3-benzyloxy-4-methoxyphenyl)-3-oxopropanoate.
            ACTIVITY - Antidiabetic; Antiarteriosclerotic; Anorectic;
     Hypotensive; Antilipemic; Nephrotropic; Neuroprotective; Ophthalmological;
     Antiulcer; Immunomodulator.
            Test details described but no results given.
            MECHANISM OF ACTION - None given.
            USE - For treatment of metabolic disorders in a subject (such as
     human) e.g. insulin resistance syndrome and diabetes including Type I
     Diabetes and Type II Diabetes; for the treatment or reduction in the
     development of atherosclerosis, arteriosclerosis, obesity, hypertension,
     hyperlipidemia, fatty liver disease, nephropathy, neuropathy, retinopathy,
     foot ulceration and cataracts associated with diabetes; and for the
     treatment of cachexia (claimed).
            ADVANTAGE - The agent effectively addresses the primary defects of
     insulin resistance and islet failure with fewer or milder side effects
     than existing drugs.
MC
     CPI: B10-C03; B10-F02; B14-D01E; B14-E11; B14-E12; B14-F02B; B14-F06;
           B14-F07; B14-J01; B14-N03; B14-N10; B14-N12; B14-N17B; B14-S04
```



ring nodes : 1 2 3 4 5 6 chain bonds : 3-10 6-7 7-8 8-18 10-11 10-12 12-13 13-14 14-15 14-16 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 exact/norm bonds : $1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 3-10 \quad 4-5 \quad 5-6 \quad 6-7 \quad 7-8 \quad 8-18 \quad 10-11 \quad 10-12 \quad 12-13$ 13-14 14-15 14-16 Match level : 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom Element Count : Node 18: Limited C, C6

2nd Shuchere Searche



chain nodes :

7 8 15 16 17 18 19 20 21 22

ring nodes:

1 2 3 4 5 6 9 10 11 12 13 14

chain bonds :

3-16 6-7 7-8 8-9 16-17 16-18 18-19 19-20 20-21 20-22

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-14 10-11 11-12 12-13 13-14

exact/norm bonds :

1-2 1-6 2-3 3-4 3-16 4-5 5-6 6-7 7-8 8-9 9-10 9-14 10-11 11-12 12-13 13-14 16-17 16-18 18-19 19-20 20-21 20-22

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS

18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:Atom

The structure I searched



PALM INTRANET

Day: Tuesday Date: 11/21/2006

Time: 10:46:16

Inventor Information for 10/532690

| Inventor Name | City | State/Country |
|--|------------------|---------------|
| HODGE, KIRVIN L. LYI | LAUREL | MARYLAND |
| SHARMA, SHALINI LYI | GAITHERSBURG | MARYLAND |
| VON BORSTEL, REID W. LUS | POTOMAC | MARYLAND |
| WOLPE, STEPHEN D. (५७ | BOYDS | MARYLAND |
| Appln Into Contents Petition Into Atty/Agent Into Continuity/Reexam Foreign Search Another: Application# Search or Patent# Search | | |
| PCT // | Search or PG PUB | |
| Bar Code # | Search | 2000 |

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CLAIMS

What is claimed is:

1. Use of a biologically active agent in the manufacture of a medicament for treatment of a condition selected from the group consisting of insulin resistance syndrome and diabetes including Type I Diabetes and Type II Diabetes; or for the treatment or reduction in the chance of developing atherosclerosis, arteriosclerosis, obesity, hypertension, hyperlipidemia, fatty liver disease, nephropathy, neuropathy, retinopathy, foot ulceration or cataracts associated with diabetes; or for the treatment of a condition selected from the group consisting of hyperlipidemia, cachexia, and obesity;

wherein the agent is selected from the group consisting of:

4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid;

Methyl 4-(4-benzyloxy-2-methoxyphenyl)-4-oxobutanoate;

Ethyl 4-(4-cyclohexylmethoxyphenyl)-4-oxobutanoate;

4-(3-chloro-4-cyclopropylmethoxyphenyl)-4-oxobutanoic acid;

Ethyl 3-(4-benzyloxyphenyl)-3-oxopropanoate;

Ethyl 3-(3-benzyloxyphenyl)-3-oxopropanoate;

Ethyl 3-(2-benzyloxyphenyl)-3-oxopropanoate;

Methyl 3-(3-(2,6-dichlorobenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(4-(4-chlorobenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(3-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(2-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(3-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-chlorophenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-methoxyphenyl)-3-oxopropanoate;

Ethyl 3-(3-benzyloxy-4-methoxyphenyl)-3-oxopropanoate;

and pharmaceutically acceptable salts thereof.

2. A method for treating a mammalian subject with a condition selected from the group consisting of insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver

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disease, cachexia, obesity, atherosclerosis and arteriosclerosis comprising administering to the subject an amount of the biologically active agent effective to treat the condition; wherein the agent is selected from the group consisting of:

4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid:

Methyl 4-(4-benzyloxy-2-methoxyphenyl)-4-oxobutanoate;

Ethyl 4-(4-cyclohexylmethoxyphenyl)-4-oxobutanoate;

4-(3-chloro-4-cyclopropylmethoxyphenyl)-4-oxobutanoic acid;

Ethyl 3-(4-benzyloxyphenyl)-3-oxopropanoate;

Ethyl 3-(3-benzyloxyphenyl)-3-oxopropanoate;

Ethyl 3-(2-benzyloxyphenyl)-3-oxopropanoate;

Methyl 3-(3-(2,6-dichlorobenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(4-(4-chlorobenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(3-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(2-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(3-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-chlorophenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-methoxyphenyl)-3-oxopropanoate;

Ethyl 3-(3-benzyloxy-4-methoxyphenyl)-3-oxopropanoate; and pharmaceutically acceptable salts thereof.

- 3. The method of claim 2, wherein the agent is administered orally.
- 4. The method of claim 2, wherein the subject is a human.
- 5. The method of claim 4, wherein the agent is administered in an amount from one milligram to four hundred milligrams per day.
- 6. The method of claim 2, wherein the condition is insulin resistance syndrome or Type II Diabetes.
- 7. The method of claim 2, wherein the condition is Type 1 Diabetes.

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8. The method of claim 2, wherein the treatment reduces a symptom of diabetes or the chances of developing a symptom of diabetes, wherein the symptom is selected from the group consisting of: atherosclerosis, obesity, hypertension, hyperlipidemia, fatty liver disease, nephropathy, neuropathy, retinopathy, foot ulceration and cataracts, associated with diabetes.

9. A pharmaceutical composition for use in the treatment of a condition selected from the group consisting of insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis, arteriosclerosis and adapted for oral administration, comprising from one milligram to four hundred milligrams of biologically active agent selected from the group consisting of:

4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid;
Methyl 4-(4-benzyloxy-2-methoxyphenyl)-4-oxobutanoate;
Ethyl 4-(4-cyclohexylmethoxyphenyl)-4-oxobutanoate;
4-(3-chloro-4-cyclopropylmethoxyphenyl)-4-oxobutanoic acid;
Ethyl 3-(4-benzyloxyphenyl)-3-oxopropanoate;
Ethyl 3-(3-benzyloxyphenyl)-3-oxopropanoate;
Ethyl 3-(2-benzyloxyphenyl)-3-oxopropanoate;
Methyl 3-(3-(4-dichlorobenzyloxy)phenyl)-3-oxopropanoate;
Ethyl 3-(4-(4-chlorobenzyloxy)phenyl)-3-oxopropanoate;
Ethyl 3-(2-(4-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(2-(2-methoxybenzyloxy)phenyl)-3-oxopropanoate; Ethyl 3-(2-(3-methoxybenzyloxy)phenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-chlorophenyl)-3-oxopropanoate;

Ethyl 3-(4-benzyloxy-3-methoxyphenyl)-3-oxopropanoate;

Ethyl 3-(3-benzyloxy-4-methoxyphenyl)-3-oxopropanoate; and pharmaceutically acceptable salts thereof.

:

10. The invention substantially as described above.

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L4
      1 ANSWERS
                 HCAPLUS COPYRIGHT 2006 ACS on STN
IC
     ICM A61K
CC
     1-10 (Pharmacology)
ΤI
     Oxocarboxylic acids and esters thereof for the treatment of metabolic
     disorders
ST
     oxocarboxylic acid metabolic disorder treatment; ester oxocarboxylic acid
     metabolic disorder treatment
IT
     Antiarteriosclerotics
        (antiatherosclerotics; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
ΙT
     Kidney, disease
        (diabetic nephropathy; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
ΙT
     Nerve, disease
        (diabetic neuropathy; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
IT
     Eye, disease
        (diabetic retinopathy; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
ΙT
     Liver, disease
        (fatty; oxocarboxylic acids and esters for treatment of metabolic
IT
        (foot; oxocarboxylic acids and esters for treatment of metabolic
        disorders)
ΙT
     Autoimmune disease
        (insulin-dependent diabetes mellitus; oxocarboxylic acids and esters
        for treatment of metabolic disorders)
ΙT
     Diabetes mellitus
        (insulin-dependent; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
ΙT
     Metabolic disorders
        (metabolic syndrome X; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
ΙT
     Diabetes mellitus
        (non-insulin-dependent; oxocarboxylic acids and esters for treatment of
        metabolic disorders)
IT
     Drug delivery systems
        (oral; oxocarboxylic acids and esters for treatment of metabolic
        disorders)
IT
     Antiarteriosclerotics
     Antidiabetic agents
     Antihypertensives
     Antiobesity agents
     Antiulcer agents
     Arteriosclerosis
     Atherosclerosis
     Cachexia
     Cataract
     Diabetes mellitus
     Drug delivery systems
     Human
     Hypertension
     Hypolipemic agents
     Obesity:
        (oxocarboxylic acids and esters for treatment of metabolic disorders)
IΤ
     Hyperlipidemia
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
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(oxocarboxylic acids and esters for treatment of metabolic disorders) ΙT Foot (ulcer; oxocarboxylic acids and esters for treatment of metabolic disorders) ΙT 39208-08-7 13335-57-4 53090-45-2 60525-32-8 63539-02-6 73083-19-9 74362-73-5 74362-70-2 77513-51-0 102513-61-1 202577-82-0 371251-24-0 373596-81-7 373596-82÷8 373596-84-0 387844-34-0 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oxocarboxylic acids and esters for treatment of metabolic disorders)

ALL ANSWERS HAVE BEEN SCANNED

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Similar Structures from Inventor

=> d scan

4 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN L6

ΙN Benzenebutanoic acid, 4-(cyclohexylmethoxy)-γ-oxo-, ethyl ester

(9CI)

MF C19 H26 04

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 4 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Benzenebutanoic acid, 2-methoxy-γ-oxo-4-(phenylmethoxy)-, methyl ester (9CI)

MF C19 H20 O5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 4 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

ΙN Benzenebutanoic acid, 3-chloro-4-(cyclopropylmethoxy)-γ-οxo-(9CI)

MF C14 H15 C1 O4

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 4 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Benzenebutanoic acid, 3-chloro-\gamma-oxo-4-(phenylmethoxy)-

(9CI)
MF C17 H15 C1 O4

$$\begin{array}{c|c} \text{O} & \text{O} \\ \text{C-} \text{CH}_2\text{-}\text{CH}_2\text{-}\text{CO}_2\text{H} \\ \\ \text{Ph-} \text{CH}_2\text{-}\text{O} \end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

Chem Drzue